

SHORT REPORT

IgA producing primary intracerebral lymphoma

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Abstract

The first case of a primary and solitary IgA (lambda) producing tumour (possibly a non-Hodgkin's lymphoma) in the CNS is reported. Clinical and neuroimaging findings are described. Early diagnosis without brain biopsy and successful therapy were possible by CSF and serum immunoglobulin analysis which proved local paraprotein production restricted to the CNS.

Intracranial manifestations of immunoglobulin producing tumours may occur in plasmacytoma and B cell type non-Hodgkin's lymphoma (NHL). Solitary intracranial tumours of this origin are rare. In particular, primary intracerebral IgA producing tumours have not yet been described to our knowledge. Early diagnosis of primary intracerebral lymphoma is difficult but essential as the prognosis appears rather favourable if proper treatment is provided. We report a patient with local production in the CNS of monoclonal IgA (lambda) due to multiple intracerebral tumour manifestations, probably of B cell NHL origin, where diagnosis was possible *intra vitam*.

Case report

A 30 year old female patient presented initially with left sided hemiparesis and hemihypoesthesia, predominantly in the leg. Symptoms had arisen following a case of mild acute pharyngitis and were rapidly progressive within a few days. After admission she also developed hemiataxia of the left side. Otherwise, her clinical status and routine laboratory examinations including HIV testing were normal.

CT showed only a small area of decreased density in the right hemisphere mainly involving the dorsal part of the internal capsule. On MRI a larger area of 4 cm in diameter appeared involved. Also, multiple small tumours could be seen in both hemispheres. There was inhomogeneous contrast media enhancement only in the large manifestation of the right side previously identified on CT (fig 1).

CSF analysis revealed a normal cell count, cytological examination, total protein, as well as normal IgG and IgM values. CSF IgA was increased to 16.2 mg/l. Hence, IgA CSF/serum quotient was raised to 9.5 (values at control examination 5 weeks after initial CSF analysis: 36.0 mg/l and 18.0, respectively). According to

the IgA evaluation graph¹ this indicates a massive and isolated CNS local production of 11.3 mg/l IgA (= 70% of total CSF IgA) and 30.6 mg/l IgA (= 85% of total CSF IgA), respectively (fig 2). By immunofixation² of 100-fold concentrated CSF the IgA could consistently be precipitated with anti-lambda but not with anti-kappa antiserum at successive lumbar punctures. Thus it was classified as monoclonal IgA, lambda light chain type. (The relatively broad shape of the M gradient is not uncommon in IgA and probably due to IgA polymers.) In addition, free lambda light chains (Bence Jones protein) were present.

Extracerebral tumours or paraprotein production could not be found on extended laboratory examinations including serum immune electrophoresis and immunofixation, as well as x ray of the chest, skull and pelvis, abdominal sonography, thoracic and abdominal CT, isotopic scans of bone marrow, liver, spleen and thyroid gland and bone marrow biopsy. Brain biopsy was refused.

After a short treatment with corticosteroids the patient improved. Radiotherapy (40 + 10 Gy) was therefore started after which the symptoms completely disappeared, except for a slight hemiataxia. Tumours were reduced to approximately one third of the initial size on MRI, with little perifocal oedema and no contrast media enhancement. Also, IgA CSF level and IgA CSF/serum quotient were down to 9.0 mg/l and 3.9, indicating a tumour IgA fraction of only 4.1 mg/l (= 40% of total CSF IgA) (fig 2). The patient has remained stable for the past 15 months.

Discussion

Plasmacytoma can directly affect the brain in different ways: By diffuse meningeal infiltration,³ by skull lesions extending intracranially⁴ and by growing from the dura mater.^{5,6} Very rarely solitary brain parenchymal lesions occur without bony or dural attachment.^{7,8} Multiple intraparenchymal CNS effects as seen in our case are more common in non-Hodgkin's lymphoma with proliferation of less mature B cells.^{9,10,11}

The clinical diagnostic features of these tumours may vary depending on site and form of CNS involvement. Diagnosis appears comparatively easy if the CNS is affected in systemic NHL or plasmacytoma, including IgA producing tumours.^{3,4,12} However, in the case of primary and solitary CNS manifestations

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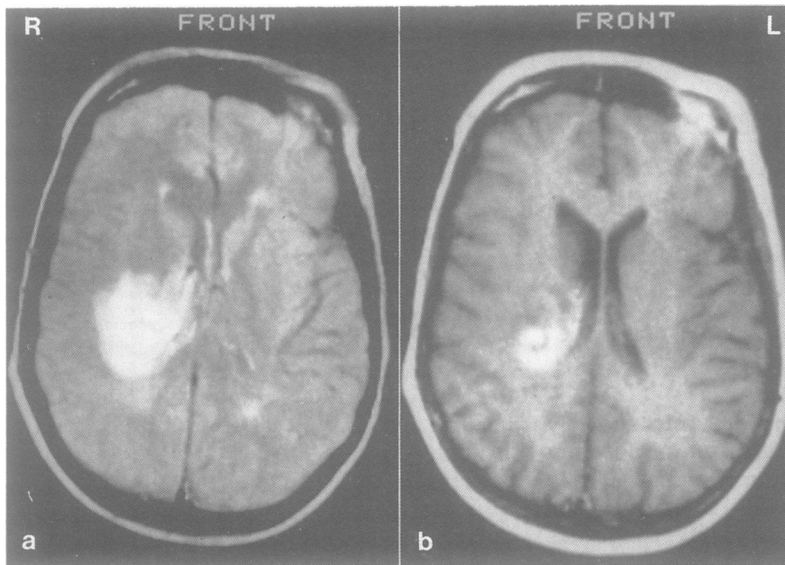


Figure 1 MRI findings before therapy (Siemens Magnetom, 1.0 Tesla): (A) T2 intermediate (TR 1.6, TE 70), without contrast media: Large hyperintense area in dorsal part of right internal capsule, in addition hyperintense nodule in left hemisphere; (B) T1 (TR 0.4, TE 30), after contrast media application (Gadolinium EDTA): Inhomogeneous enhancement only in the largest tumour manifestation of the right side.

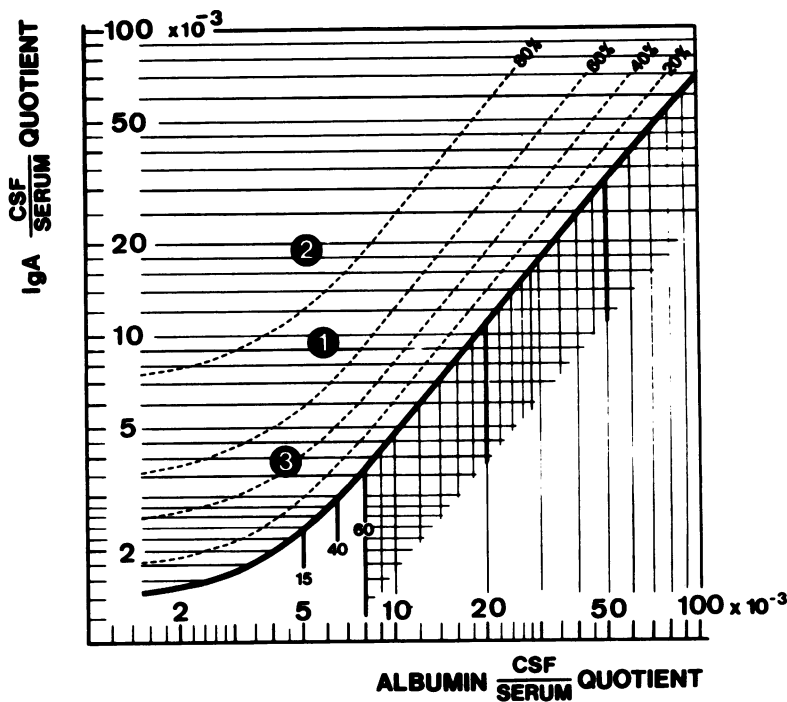


Figure 2 Local IgA production in the CSF: GSF IgA evaluation graph.¹ Values above the solid line indicate local IgA production. Dotted lines in this range permit quantitation of locally produced IgA fraction. Age dependent ranges of normal albumin quotients are marked. 1) Lumbar puncture at first presentation; 2) Values at control examination after 5 weeks (before radiation therapy); 3) Values 6 months after radiation therapy.

the diagnosis is very difficult to establish without performing brain biopsy.

Partly this is due to problems in diagnosing these tumours radiologically. The differential diagnosis of CNS plasmacytoma includes brain tumours, such as, astrocytoma, metastases and granulomatous diseases. Plasmacytoma manifestations growing from the dura mater may closely resemble meningioma on CT.⁵ In par-

ticular the CT appearance of CNS lymphomas is not uniform and by no means specific. Most frequently they appear as isodense or slightly hyperdense mass lesions with homogeneous or nodular contrast media enhancement.⁷ Hypodense structures with ring enhancement are less common⁹ and lesions without contrast media enhancement are rare.^{13 14}

As demonstrated in our case, MRI is the imaging procedure of choice in NHL as it may show lesions not detectable by CT. As in CT, we also found some degree of enhancement after contrast media administration. However, MRI is no more specific than CT.^{10 11 14}

Therefore, in solitary intracranial B cell neoplasms diagnostic proof can best be obtained by demonstration of local paraprotein production in the CNS. When sufficiently sensitive techniques are applied, at least in serum monoclonal B cell proliferation end even gammopathy can be shown in a surprisingly high percentage (81%) of patients with non-Hodgkin's lymphoma.²

In the CSF this is possible in two ways: malignant B cells, if present, can be detected by specific immunoperoxidase staining using antisera against immunoglobulins of a single class and light chain type.¹⁵ The presence of secreted monoclonal immunoglobulins can be proved by immunoelectrophoresis.^{3 4 16} anti-idiotypic antisera¹² isoelectric focusing¹⁷ or, as in our case, very sensitively by immunofixation of concentrated CSF.

It should, however, be stressed that the mere presence of a paraprotein cannot be used as proof of local production in the CSF since all serum immunoglobulins including paraproteins will enter the CSF space, although each at a different rate depending on their hydrodynamic radius and the permeability of the blood/CSF barrier. Local production can only be established by quantitative methods,¹⁷ preferably by graphical evaluation of the respective CSF/serum quotients of immunoglobulin and albumin.¹ As shown in our case, this technique also allows a close monitoring of therapeutic efficiency.

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